

## NJOY-OIRA Meeting on FDA's Final Deeming Rule

ENDS Have Tremendous Potential Benefits:

- Smoking results in \$289 billion in costs every year and 480,000 premature deaths, primarily due to the highly toxic nature of tobacco smoke as a product of combustion.
- Smoking is highly addictive: CDC data shows that only 6.2% of those who attempt to quit each year are able to do so, even with medical intervention, such as nicotine replacement therapy.
- Encouraging smokers who cannot or do not want to stop smoking to switch to ENDS could help to substantially reduce smoking related disease, death and health inequalities.
- **Transitioning smokers to ENDS could save as much as \$274.5 billion per year and as many as 456,000 lives.**

PMTA Costs Threaten Public Health Gains and the Requirements Must Be Modified:

- Based on meetings with FDA and detailed cost analysis, we show that for a first single application, the PMTA process is likely to cost approximately \$1,390,000 - \$3,240,000 (or more), not the NPRM's estimated \$325,000.
- Some costs are attributable to inappropriate requirements for post-market and population studies that should be generalizable from ENDS research already being funded by FDA and would be unnecessary for every specific ENDS.
- FDA can also reduce the PMTA burden by "application bridging": allowing manufacturers to submit applications that reference their previously approved products or representative data from their own applications and listing only information about major differences.
- **If FDA intends to set requirements for PMTA applications through Guidance, it must take comments on and finalize that document before the PMTA process goes into effect.**

Other Issues:

- **FDA should allow adult-targeted flavorings, to promote smokers' complete switching away from combustibles, to avoid dual use as an endpoint, and to prevent reversion.**

- FDA should make explicit that the TCA preempts existing and proposed State requirements, specifically including product standards, manufacturing requirements, and labeling.
- FDA must protect CBI submitted as part of the PMTA application process.
- Compliance deadlines to submit product registration and ingredient listings should remain consistent with the proposed rule.

Electronic Nicotine Delivery Systems (ENDS) are relative newcomers to market, with essentially all products appearing only after 2007. There continues to be a great deal of innovation and change in the ENDS market, and these products hold the possibility of extremely large benefits to the public health. NJOY's mission is to make cigarette smoking obsolete, with concomitant reductions in the morbidity and mortality caused by cigarette smoking.

NJOY supports balanced FDA regulation of ENDS and encourages the agency to finalize the rule as soon as possible. We firmly believe that establishing basic product standards, registering manufacturers and products, and curbing youth access are all important goals. We are eager to work with FDA to achieve those goals.

We are concerned, however, that the premarket review process envisioned by FDA has the potential to unnecessarily hamper innovation in the ENDS marketplace and deliver the category to the control of legacy Big Tobacco companies. FDA's proposed rule contained little specific information about information manufacturers would be required to submit to obtain an approval. NJOY met with FDA on this topic in Q2, 2015, to seek scientific advice from CTP's Office of Science regarding an investigational plan and information needed to support PMTAs for NJOY products. Based on the specific advice received, NJOY unequivocally concludes that filing a PMTA will be significantly more expensive than the proposed rule estimated.

This input, together with a subsequently leaked FDA guidance document specific to ENDS, confirms the need for improvements to be made to the PMTA process and related expectations that can ensure its workability, for FDA, manufacturers (including independents), and in the interests of public health.

## **Potential Benefits of ENDS**

There are tremendous potential public health benefits from transitioning smokers away from traditional, combustible products to ENDS, and FDA has an unprecedented opportunity to make enormous public health gains by regulating appropriately. As the Agency correctly

notes, the human and financial tolls of smoking are vast: each year, an estimated 480,000 deaths can be attributed to cigarette smoking, along with \$133 billion in annual health care expenses and \$156 billion in annual lost productivity.<sup>1</sup>

Unfortunately, smoking cessation efforts have very low success rates – even with interventions like counseling and nicotine replacement therapy. CDC research indicates that only about 6.2% of those who tried to quit smoking in the prior year were successful at doing so.<sup>2</sup> For the vast majority of consumers, becoming addicted to smoking means continuing smoking and all the serious attendant health consequences.

Many smokers have found that using ENDS allows them to taper off or discontinue their smoking altogether, and the scientific evidence thus far indicates that complete substitution by smokers is likely to be of large benefit to public health.

FDA has repeatedly acknowledged that tobacco products exist on a continuum of risk and that each product must be regulated in an appropriate fashion; however, the Agency failed to provide any evidence about the actual risk level associated with ENDS in its proposed rule. That is partially because the category of product is so new that a sufficient body of long-term evidence does not yet exist – though, to be clear, there is a robust amount of laboratory data characterizing the emitted vapor from ENDS products. FDA requested comment on this topic and has been conducting a series of listening sessions to learn more about potential risks of ENDS. While we support these efforts to acquire more data, we urge the Agency not to take punitive action against the industry in its final rule – particularly when the costs of doing so (in terms of foregone public health benefits) very possibly outweigh the benefits of draconian regulation by orders of magnitude.

Although the long-term risks of ENDS use remain, necessarily, unknown, there is very good reason to believe that they are extremely low by comparison to traditional tobacco products. Most of the risk of cigarette use is tied to the various products of combustion that are present. With ENDS, no combustion takes place and that portion of risk is thereby mitigated.<sup>3</sup>

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<sup>1</sup> United States Department of Health and Human Services (USDHHS). The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2014.

<sup>2</sup> "Quitting Smoking Among Adults – United States, 2001-2010," Morbidity and Mortality Weekly Report, Vol 60(44), November 2011.

While it might seem obvious that ENDS pose a lower risk, some initial work has attempted to quantify the difference. Nutt et al. (2014) performed a guided elicitation of public health experts to assess their sense of the risks posed by ENDS.<sup>4</sup> While the experts did not agree that ENDS posed no risk at all, their estimation was that the potential harms resulting from ENDS use were approximately 5% of those that might result from cigarette smoking.

We acknowledge that an expert elicitation has inherent limitations and does not take the place of longitudinal studies. Nutt's results should be considered only with significant uncertainty and awareness that there may be error bars around the paper's conclusions. But in the absence of firmer long-term data, we believe that experts' estimates are useful information that FDA must take into account. And what Nutt demonstrates is that there are potentially vast benefits to transitioning smokers to ENDS.

Most promisingly, Public Health England, the UK agency charged with protecting the public health, released a recent study looking at the health effects of vaping and ENDS.<sup>5</sup> That study also found that ENDS are of substantially lower risk than combustible cigarettes and have the potential to be of tremendous public health benefit. While this is an area where research is still developing, the initial data seem to agree that these products are much, much less risky than cigarettes. Indeed, at this point, even committed ENDS skeptics – including Dr. Tom Frieden of the CDC, the WHO, the American Heart Association, UCSF Professor Stan Glantz, and others -- uniformly agree that ENDS appear to pose lower risk to individual smokers than combustion cigarettes and that a smoker who cannot or will not quit is making a positive health choice by switching completely to ENDS.

As an upper-bound exercise in determining maximum benefits, consider the result if all cigarette smokers transitioned to ENDS users at 5% of the total harm. That implies a reduction in annual deaths of 456,000 and a reduction in annual costs of \$274.5 billion. Or say that the expert elicitation is too low by an order of magnitude and that the health consequences are only half as severe as cigarettes. Further, say

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3 We are aware that some studies show that using ENDS beyond normal usage conditions may offer less reduction in risk. We believe that these issues can and should be solved with basic product standards and cGMPs, as described in a later section of these comments.

4 Nutt, et al., "Estimating the Harms of Nicotine-Containing Products Using the MCDA Approach." European Addiction Research, 2014;20: 218-225.

5 McNeill, et al, "E-cigarettes: An Evidence Update." Public Health England, August 2015. Available at: [https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/457102/E-cigarettes\\_an\\_evidence\\_update\\_A\\_report\\_commissioned\\_by\\_Public\\_Health\\_England\\_FINAL.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/457102/E-cigarettes_an_evidence_update_A_report_commissioned_by_Public_Health_England_FINAL.pdf)

that only half of smokers transition to ENDS. Even under those much less charitable assumptions, switching to ENDS has the potential to avert 120,000 deaths and \$72.3 billion in costs every year.

We present these scenarios not to make linear public health projections, but to illustrate the reality that the potential benefits of having ENDS on the marketplace as a means of displacing cigarettes vastly outweighs any of FDA's projected benefits from regulating ENDS. Again, while we support sensible ENDS regulation, it is vital to take this into account when considering provisions that might fundamentally disrupt the ENDS market, as the premarket approval requirements, under FDA's apparent current interpretation, are very likely to do.

### **FDA's PMTA Process**

It has proven difficult to assess exactly what FDA's proposed requirements for a PMTA will be. Instead of including the details of the required information in the proposed rule, FDA apparently intends to set those requirements at a later time through the use of guidance documents. Because the exact requirements of a PMTA are of utmost importance in determining the costs and feasibility of compliance with the proposed rule, it has been difficult to assess and comment on, as well as difficult to establish appropriate research and development plans to meet such expectations. In an attempt to address this uncertainty, NJOY met with CTP's Office of Science earlier this year regarding FDA's expectations for the submission of an ENDS PMTA. We appreciated the opportunity to meet with FDA on this topic and we believe that the conversation allows us to comment with unusual precision on the costs of that process.

Based on our meeting with FDA, we prepared an analysis of all the items that we believe CTP intends to require as part of a complete PMTA application, along with the associated costs of each item. Our analysis is, in most ways, consistent with the recently leaked FDA Guidance document on PMTAs for ENDS (although the Guidance contains some provisions that are potentially excessive). In either case, it is clear that meeting FDA's expectations will be dramatically more expensive than the proposed rule's estimates of 5,000 hours, or approximately \$325,000. After extensive analysis of our meeting with CTP, we estimate that the true cost for an initial PMTA for a single product may be closer to (conservatively) \$1,393,000 per initial application.

We are also concerned that the leaked guidance document implies a process significantly more burdensome and extensive than our current understanding. It suggests that FDA might require, for example, *in vivo*

animal testing of products and multiple human clinical trials to evaluate health outcomes – more akin to expectations for medicinal products. We have also calculated the likely costs of including these additional requirements with a PMTA application and believe that they would raise the cost to more than \$3.2 million per initial application, a figure that we do not believe would be sustainable (see attached cost calculations).

### **Potential Unintended Consequences of FDA Regulation**

Clearly there are scenarios under which the PMTA process could become excessively burdensome and costly in cost and time. If FDA's application process becomes excessively costly (for instance, by requiring *in vivo* animal testing) or excessively slow (for example, by repeated requests from FDA for additional data and information), the PMTA could become either a de facto ban on ENDS or a hurdle so high that only legacy Big Tobacco companies could clear it. Neither of those outcomes would be justified by the evidence or in the interests of public health.

The Big Tobacco companies are unlikely to have the same incentives to innovate in the ENDS space, as doing so would be likely to cannibalize their existing consumer base for combustible products. In fact, these companies would likely have a strong incentive not to improve vaping products in hopes of preventing more users from entirely leaving smoking. NJOY submits that this outcome would not be appropriate for the protection of public health.

A de facto ban on ENDS would also clearly not be in the interest of public health. A failure on the part of the Agency to review and approve PMTAs in a timely manner or to set reasonable expectations for the approval of PMTAs could lead to the withdrawal of ENDS from the marketplace and, with them, the extremely large potential benefits to be garnered from moving smokers away from combustible products. Although CTP had not previously acted on any PMTAs for already-deemed tobacco products, we noted with appreciation that the Agency granted its first approvals last week. NJOY was pleased to see this sign of progress.

### **A More Workable PMTA Process**

The PMTA process must not be more burdensome than necessary. At minimum, we believe FDA should incorporate the suggestions below.

*Finalize Guidance*

As we have discussed, it has been difficult for ENDS manufacturers to intelligently comment on the proposed Deeming rule because FDA apparently intends to codify many of the most important provisions for the PMTA application process in a subsequent Guidance document. We believe that using Guidance documents in this way potentially violates the Administrative Procedure Act and undermines the regulatory process. While the advice that NJOY has received from CTP's Office of Science has been helpful, we are concerned that the final process has the potential to be more extensive than is truly necessary.

If FDA intends to formalize the PMTA application requirements through Guidance documents, we believe that the Agency must at a minimum commit in the final rule to taking comment on and finalizing that Guidance document before the PMTA provisions can go into effect.

#### *Allow Bridging*

Second, we believe that the Agency should allow “bridging” between a company’s approved products and its subsequent applications. A company should not be expected to duplicate the high upfront costs for an initial PMTA application for each innovation or improvement to its own products. We believe that FDA can provide some regulatory relief by allowing manufacturers to reference their approved applications in subsequent PMTA filings. Under this scenario, when a manufacturer submits an application for a similar product, they could simply reference their already-approved application adding only data and information relating to the characteristics that differ from the approved product. Such bridging would significantly reduce burden on manufacturers but would still provide FDA with exactly the same level of information.

#### *Do Not Include Unnecessary Requirements*

Based on our conversations with CTP staff, we do not believe that FDA intends to require the submission of any of the following information as a part of PMTA applications. NJOY believes that requiring this information would be inappropriate and would likely drive the cost of the application to an unsustainable \$3.2 million or greater.

- *In Vivo* toxicology studies
  - o These studies could cost at least \$300,000 and potentially up to approximately \$4,000,000 depending on scope, such as multiple species and long durations.
  - o Extensive work in multiple in vitro models has already been published showing that ENDS have lower toxicity than combustion cigarettes. These studies apply to a wide

scope of ENDS products and justify the unnecessary time, expense, and complication of in vivo animal studies.

- Neilson et al 2015 Toxicology in Vitro showed that e-cigarette aerosol generated no decrease in cell viability or cell membrane barrier function in a culture of human tracheal/bronchial epithelial cells, whereas cigarette smoke produced major decreases in both attributes.
  - Goniewicz et al 2014 Tobacco Control used multiple analytical chemistry techniques to analyze the chemical composition of e-cigarette aerosol, showing that the content of hazardous components ranged from 9 to 450-times lower in e-cigarette aerosol compared to combustion cigarette smoke.
  - Farsalinos et al 2013 Internal Journal of Environmental Research and Public Health explored the effects of e-cigarette aerosols on myocardial cells and found they were significantly less cytotoxic than cigarette smoke extract.
  - Romagna et al 2013 Inhalation Toxicology probed cell viability in mice fibroblasts, with the conclusion that e-cigarette aerosols had substantially lower cytotoxicity than combustion cigarette smoke extract.
  - Cervellati et al 2014 Toxicology in Vitro assessed cytotoxicity and inflammatory marker in keratinocyte skin cells and lung epithelial cells, concluding that while e-cigarette aerosols may produce some effects, they are far less toxic than combustion cigarette smoke.
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- Manufacturer-initiated studies of initiation, cessation, switching behaviors, etc.
    - o Such studies would cost at least \$600,000 and could take up to a year or more. FDA is already investing substantial funds to generate such data via studies such as PATH, and via regulatory collaborating centers. Much of these data should be generalizable without the need for individual manufacturers to bear unnecessary and repetitive cost burden.
  - Manufacturer-initiated studies of human health outcomes
    - o Such studies would cost at least \$500,000 and take multiple years. ENDS as regulated by FDA's Center for

Tobacco Products are not medicines with health claims. While it is clearly of academic interest to evaluate multiple potential health outcomes, such research is better justified as necessary for products seeking medicinal approval rather than as alternative tobacco products.

## **Other Critical Issues**

### *Flavors*

NJOY has only recently expanded its flavor offerings to include a wide variety of tastes for consumers. For most of our history, we focused on traditional tobacco and menthol flavorings. We decided to begin offering more flavor choices for a simple reason: consumer research shows that smokers who have the opportunity to migrate to flavors other than tobacco or menthol appear more likely to completely switch to ENDS and less likely to either engage in dual use as an endpoint and/or to revert to combustibles later. We view adult-targeted flavor offerings as a key part of our mission to obsolete cigarettes.

An online survey of former smokers (attached) showed us that most respondents (69%) reported that restricting flavor variability would make ENDS less enjoyable and over a third (40%) said that they would have been less likely to reduce or quit smoking with flavor restrictions. These findings highlight the importance of flavor variety in facilitating a complete move from combustible cigarette use to ENDS use.

That said, while NJOY believes that flavors can be useful in helping adults to transition away from cigarette use, we strongly oppose the use of flavors that are designed to appeal to non-smoking youth. NJOY was concerned about the possibility that flavorings might lead to youth uptake and commissioned a study to determine their effect.<sup>6</sup>

We have attached the full study for your review, but each participant completed an online questionnaire assessing his or her interest in ENDS across 15 flavor descriptors. The flavor descriptors included both traditional tobacco (classic tobacco, menthol, dark tobacco blend) and other (black & blue berry, blood orange, bubble gum, butter crunch, cotton candy, double espresso, gummy bear, peach tea, pomegranate, raspberry, single malt scotch, vanilla bean) flavor types. Of note, the flavors of bubble gum, cotton candy, and gummy bear were then (and remain) **not** under consideration by NJOY, but the authors included them to evaluate whether descriptors that reference

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<sup>6</sup> Saul Shiffman, *The Impact of Flavor Descriptors on Nonsmoking Teens' and Adult Smokers' Interest in Electronic Cigarettes*, 17 Nicotine & Tobacco Res., available at <http://ntr.oxfordjournals.org/content/early/2015/01/24/ntr.ntu333>

products assumed to be consumed by youth would have teen appeal in the context of an ENDS product. They found that

- Many ENDS flavors appealed to adult smokers without appealing to nonsmoking teens;
- Non-smoking teens' interest in using ENDS did not vary according to which flavor descriptor is associated with the ENDS.

We do not support the use of flavor descriptors that appeal disproportionately to youth, but we ask that FDA approach this issue using rational, evidence-based policymaking. NJOY believes that a choice of ENDS flavors can help adults to completely transition away from smoking and, thus, that they have large potential public health benefits.

A preliminary report of research conducted by Georgia State University Tobacco Center of Regulatory Science, an FDA collaborating center, highlights the role of enjoyment for ENDS products. (Unpublished data 2014 GSU Tobacco Products and Risk Perceptions Survey). Those smokers who completely switched to ENDS had substantially higher ratings of enjoyment for ENDS than those who were dual users of both ENDS and continued to smoke. This suggests that enjoyment is a critical component of achieving the preferable health outcome.

Risks of flavoring can be mitigated to ensure that they are not disproportionately appealing to youth. Should FDA choose to regulate or otherwise restrict the use of ENDS flavors, we strongly recommend that the Agency not do so on a one-size-fits-all model. More than 300 companies have already publicly committed (see [www.vapefreeyouth.com](http://www.vapefreeyouth.com)) to ensure that flavors target adult smokers only and to the development of a sensible protocol to ensure flavors used are not being used to target children. FDA has an opportunity to work with industry and others to generate evidence based guidance on such an approach and NJOY and other companies stand ready to assist as appropriate. Such a protocol could require consumer research data that demonstrates flavored products are not disproportionately appealing to youth and thereby unlikely to lead to youth initiation. This could take into account many different factors that might lead to youth appeal – including packaging, lettering, color, flavor descriptions, ad copy, distribution media, and any other criteria deemed appropriate by the Agency.

#### *Preemption*

When issuing the final deeming regulation, FDA must make clear that, upon the regulation's effective date, the Federal Food, Drug, and Cosmetic Act (FFDCA) will preempt all state and local requirements relating to (among other subjects) package labeling, product standards unrelated to fire safety, and good manufacturing standards applicable to deemed tobacco products, unless such requirements mirror federal requirements. The FFDCA's preemption provision applies to state and local requirements both "different from, or in addition to" FFDCA requirements related to such standards and labeling requirements:

No State or political subdivision of a State may establish or continue in effect with respect to a tobacco product any requirement which is different from, or in addition to, any requirement under the provisions of this subchapter relating to tobacco product standards, premarket review, adulteration, misbranding, labeling, registration, good manufacturing standards, or modified risk tobacco products.<sup>7</sup>

Thus, once ENDS are deemed, the law will automatically preempt all such state and local standards and labeling requirements.

Numerous states and local governments have already established and continue to consider such laws, creating a growing patchwork of often-inconsistent requirements for ENDS products – often with little advance notice and invariably without undertaking any meaningful, unbiased consideration of applicable science or data. By not acknowledging the preemptive effects of the deeming regulation, FDA would create unnecessary confusion regarding state and local governments' inability to enforce existing and establish new requirements for deemed products. This confusion would needlessly and significantly burden businesses by forcing them to choose whether to:

- Produce different products for different markets (e.g., to comply with different warning statement requirements, manufacturing requirements, and/or flavor bans);
- Expend substantial resources to clarify state and local authorities' enforcement plans and, where necessary, seek judicial declarations confirming the preemptive effect of the deeming regulation; or

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<sup>7</sup> 21 U.S.C. § 387p(a)(2)(A). The preemption provision contains an "exception" clause that does not preempt state and local requirements "relating to the sale, distribution, possession, information reporting to the State, exposure to, access to, the advertising and promotion of, or use of, tobacco products by individuals of any age, or relating to fire safety standards for tobacco products." 21 U.S.C. § 387p(a)(2).

- Market products at risk of attempted enforcement of preempted state and local requirements.

FDA's own prior statements on this issue have made the need for Agency confirmation of the preemptive effect greater still. In particular, in the preamble to its deeming proposal, FDA inaccurately stated that, in conducting its required federalism analysis, "FDA has not identified any State or local laws that would be preempted by these proposed restrictions."<sup>8</sup> Contrary to FDA's statement, in April 2014, such preempted state and local laws (most notably, California's Proposition 65<sup>9</sup> and its implementing regulations) already existed, and the patchwork continues to expand today.<sup>10</sup> FDA's required federalism analysis must accurately reflect the preemptive effect of the deeming regulation and correct the record regarding its impact on the growing patchwork state and local laws.

#### *Confidential Business Information*

NJOY is committed to work with FDA to ensure that they have the information necessary for the protection of public health. We believe, however, that FDA should formally commit to protecting any confidential business information that is submitted through the PMTA process and should not make public data or other information that might disadvantage applicants.

However FDA finalizes the PMTA application process, it will necessarily involve the disclosure to FDA of a great deal of confidential business information. As we have noted, NJOY estimates that a single initial application is likely to cost in the range of at least \$1,393,000. Allowing a manufacturer to reference its previously approved PMTAs and to submit only information pertaining to relevant changes would significantly reduce the company's burden while still providing FDA with the information it needs. Making approved PMTAs, or the confidential information therein, public, however, would be both inappropriate and inconsistent with applicable law. As required under the Federal Food, Drug, and Cosmetic Act, FDA should protect CBI submitted as part of a PMTA at all times.

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<sup>8</sup> 79 Fed. Reg. 23,142, 23,195 (April 25, 2014).

<sup>9</sup> Cal. Health & Safety Code § 25249.6.

<sup>10</sup> E.g., Ind. Code §§ 7.1-7-4-6, 7.1-7-5-1 (establishing packaging requirements, labeling requirements, manufacturing requirements, and ingredient restrictions for e-liquids); Utah Code § 26-57-103 (requiring the promulgation of, and compliance with, regulations establishing standards for the labeling, nicotine content, packaging, and product quality of unsealed "electronic cigarette substances"); El Cerrito (CA) Code § 6.100.160 (banning the sale of flavored tobacco products, including e-liquids).

### *Compliance Dates*

As described above, we believe that FDA's requirements with respect to PMTAs should not go into effect until FDA has taken comment on and finalized its draft guidance setting out the information requirements for an application. With that exception, NJOY supports FDA's proposed deadlines for compliance with all other provisions of the rule.

## **Appendix: Additional Supporting Evidence**

For your convenience, we have attached several additional documents which we believe will provide you with useful evidence and factual support during your review.

- A) Industry Self-Regulation document: Statement of Principles
- B) RJ Reynolds et al. v Hamburg: Striking down FDA's final Graphic Warning Labels rule
- C) Study on efficacy of flavored ENDS at reducing smoking rates
- D) NJOY's full comments, submitted to FDA
- E) Provision-by-provision analysis of costs of PMTA, as based on extensive discussion with CTP
- F) CDC study on rates of successful smoking cessation (available at <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6044a2.htm>)
- G) 2015 Public Health England study finding that ENDS can be of large public health benefit (available at <https://www.gov.uk/government/publications/e-cigarettes-an-evidence-update>)
- H) Nutt, 2014: Elicitation demonstrating that experts believe ENDS to be about 95% less harmful than conventional, combustible

- cigarettes. (available at  
<https://www.karger.com/Article/FullText/360220>)
- I) SBA's publicly filed comments on the Proposed Deeming rule (<https://www.sba.gov/content/61114-deeming-tobacco-products-be-subject-federal-food-drug-and-cosmetic-act-amended-family-smoking-prevention-and-tobacco-contr>)
  - J) Saul Shiffman, The Impact of Flavor Descriptors on Nonsmoking Teens' and Adult Smokers' Interest in Electronic Cigarettes, Nicotine & Tobacco Res., available at <http://ntr.oxfordjournals.org/content/early/2015/01/24/ntr.ntu333>
  - K) Slide reporting finding from research re Human Decision Making About Tobacco Products: Experience of using e-cigarettes compared to smoking regular cigarettes – Presented at The Food and Drug Law Institute - October 21, 2015. Michael P. Eriksen, ScD, Dean, School of Public Health, Georgia State University.
  - L) Industry Self-Regulation document: Statement of Principles (available at <http://www.vapefreeyouth.com/>)
  - M) RJ Reynolds et al. v Hamburg: Striking down FDA's final Graphic Warning Labels rule (available at [https://www.cadc.uscourts.gov/internet/opinions.nsf/4C0311C78EB11C5785257A64004EBFB5/\\$file/11-5332-1391191.pdf](https://www.cadc.uscourts.gov/internet/opinions.nsf/4C0311C78EB11C5785257A64004EBFB5/$file/11-5332-1391191.pdf))
  - N) Study on efficacy of flavored ENDS at reducing smoking rates (Farsalinos) <http://www.mdpi.com/1660-4601/10/12/7272>